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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/838,987	Applicant(s) CHAMBERLAIN ET AL.	
	Examiner Michael Wilson	Art Unit 1632	

-- The MAILING DATE of this communication appears on th cover sh t with th correspondence addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

DETAILED ACTION

Applicant's arguments filed 6-14-02, paper number 6, have been fully considered but they are not persuasive. Claims 1-20 remain pending in the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The first line of specification need updated to indicate 09/171086 has been abandoned.

The specification does not describe Fig. 1B-1E (page 5). Applicants argue page 5 does not have to describe Fig. 1B-1E because they are generically described on page 5 in the description of Fig. 1, as well as in Example 1, pg 21-23. Applicants argument is not persuasive. The Brief Description of the Drawings must include a description of each drawing. Since Fig. 1A-1E are each separate drawings, they must all be described in the Brief Description of the Drawings.

Claim Rejections - 35 USC § 112

1. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The limitation of immunizing against any "antigen-associated disease" is new matter. The scope of "antigen-associated disease" is not defined in the specification or the art at the time of filing.

The scope of "immunizing" against any "antigen-associated disease" was not contemplated in the specification as originally filed.

The limitation of immunizing against "an antigen-associated disease" and inducing an immune response against "at least one antigen" does not have support in the specification as originally filed. The immunization does not induce an immune response against more than one antigen as encompassed by "at least one antigen".

2. Claims 1-20 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of enhancing a CTL response in a mammal comprising administering a vaccinia viral vector encoding an antigen operably linked to a promoter followed by administering a fowlpox vector encoding said antigen operably linked to a promoter such that an enhanced CTL response against said antigen occurs as compared to vaccinia followed by vaccinia, fowlpox followed by fowlpox or fowlpox followed by vaccinia, does not reasonably provide enablement for obtaining an enhanced immune response using any combination of vectors as broadly claimed or treating cancer as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for reasons of record.

Claim 1 does not have an enabled use as written because merely "inducing an effective immunological response thereby immunizing the mammal against the antigen associated disease" in context of the specification is not necessarily prophylactic or therapeutic. The specification

teaches obtaining immune responses using the claimed invention that do not treat or prevent disease (e.g. vectors encoding β-gal). The only disclosed purpose for obtaining an immune response against β-gal is for further study to find methods of vaccination that generate a CTL or antibody response that is therapeutic or prophylactic (pg 4, lines 2-13).

Claims 1-8 are directed toward "immunizing a mammal against an antigen-associated disease inducing an effective immunological response against at least one antigen in the mammal." Claims 1-8 encompass treating or preventing disease because the purpose of the invention is to treat or prevent disease (pg 1, line 3; pg 4, line 17). Claims 9-20 are directed toward treating cancer and result in producing an effective immune response against the cancer in the patient.

It was known in the art that a CTL response against β-gal could be induced upon administering wild-type vaccinia followed by a fowlpox vector encoding β-gal (Wang, 1995, J. Immunol., Vol. 154, pages 4685-4692). Administering wild-type fowlpox followed by vaccinia virus encoding β-gal also provided a CTL response against β-gal (pg 4689, col. 2, last sentence).

It was also known in the art at the time of filing that the combination of vector, promoter, antigen, target tissue, level of expression and route of administration required to target the desired tissue and obtain a therapeutic or prophylactic effect using gene therapy was unpredictable (Miller, 1995, FASEB J., Vol. 9, pages 190-199; pg 198, col. 1; Deonarain, 1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69; pg 53, first para., pg 65, first para. under

Conclusion; Verma, Sept. 1997, Nature, Vol. 389, pages 239-242; see entire article, pg 240, sentence bridging col. 2-3; Crystal, 1995, Science, Vol. 270, pg 404-410; pg 409).

The specification demonstrates administering a vaccinia, fowlpox or plasmid vector encoding β-gal followed by a different boosting vector encoding β-gal and obtaining a CTL response against β-gal as compared to vaccinia followed by vaccinia or fowlpox followed by fowlpox (page 25, Ex. 2). The specification discusses various viral vectors (pg 9-10) and various antigens (pg 11-13) to treat a variety of diseases including cancer (pg 11, lines 11-35). Example 1 teaches increasing survival of mice having β-gal-expressing tumors using vaccinia followed by fowlpox or fowlpox followed by vaccinia, each of which encode β-gal (page 21; Fig.1) and contemplates administering vectors encoding tumor associated antigens (TAA) against melanoma (example 5). The specification does not provide adequate guidance to treat cancer as claimed because the β-gal tumors do not correlate to tumors having tumor associated antigens. β-gal does not correlate to any TAA because it is a foreign protein while TAAs are self-proteins, because β-gal and TAAs known in the art do not have the same epitopes recognized by the immune system, β-gal and TAA have different MHC restriction and because β-gal and TAAs ability to induce immunity differ. Specifically, the specification does not provide any guidance to treat cancer using MART-1, gp100, TRP-1 or TRP-2 because the specification does not correlate the epitope of β-gal is the same amino acid sequence and structure as epitopes of MART-1, gp100, TRP-1 or TRP-2, that MART-1, gp100, TRP-1 or TRP-2 are H-2L^{d} -restricted, or that MART-1, gp100, TRP-1 or TRP-2 induce an equivalent immune response as β-gal.

Thus, the specification does not provide adequate guidance for one of skill to administer a vector to a mammal and treat cancer by teaching the level of expression of antigen required to induce the desired immune response, how to target antigen expression to the desired tissue such that the desired immune response is obtained, or by correlating β-gal to tumor antigens such as MART-1, gp100, TRP-1 or TRP-2. Given the state of the art at the time of filing taken with the teachings in the specification, it would require one of skill undue experimentation to determine the dosage, route of administration, vector, promoter, antigens, target tissue or level of antigen expression required to obtain the desired immune response and treat cancer as claimed.

Applicants argue pg 4, lines 2-13, teach using the injection strategy claimed to treat cancer, infectious disease, autoimmune disease, or fungus or virus-related disease. Applicants argument is not persuasive because the specification does not overcome the unpredictability in the art by teaching the specific parameters required to use the invention to treat disease.

Applicants argue Example 2, pg 25, teaches the combination of vectors required to enhance the immune response. Applicants argument is not persuasive. The claims no longer require enhancing the immune response. Example 2 does not enable treating cancer because tumors expressing β-gal do not correlate to tumors expressing tumor antigens for reasons cited above.

Applicants argue Cooney and Graham taught using vaccinia encoding HIV gp160 as a vaccine, and Estin used vaccinia encoding p97 melanoma antigen. Cooney and Graham do not teach treating or preventing HIV. Estin did not teach treating or preventing melanoma.

Applicants argue that one of skill in the art would use an antigen specific to the tumor being treated (pg 5, para. 3, lines 1-5, of arguments). Applicants argument is not persuasive. As stated above, the combination of vector, promoter, target tissue, level of expression and route of administration required to target the desired tissue and obtain a therapeutic or prophylactic effect using gene therapy was also unpredictable. The specification does not teach the specific vector, promoter, target tissue, level of expression and route of administration required to target the desired tissue and obtain a therapeutic or prophylactic effect against a specific type of tumor using a vector encoding an antigen known to be associated with the tumor.

Applicants argue pg 29, Example 5, enables treating melanoma. Applicants argument is not persuasive. Example 5 does not teach the specific combination of vectors, the promoter, level of expression of pg100 or MART-1, or route of administration required to target melanoma and obtain a therapeutic or prophylactic effect against melanoma.

The specification does not enable using vectors encoding antigens as well as immunostimulatory molecules (cytokine, growth factor or a co-stimulatory molecule) to treat cancer. Vieweg (1995, Cancer Investigation, Vol. 13, pages 193-201) taught it was unpredictable what combination of cytokine was required for what tumor (page 198, column 1, line 1). The specification fails to enable using such a vector to treat cancer by teaching the level of expression required, how to obtain the desired level of expression using gene therapy or the combination of cytokine to use with an antigen to treat cancer.

Applicants argue pg 18, lines 11-25 provide adequate guidance to treat cancer using the invention when the vectors addition encode an immunostimulatory molecule. Applicants argument is not persuasive. The teachings on page 18 are not specific. The teachings on pg 18 are not adequate for one of skill in the art to overcome the unpredictability in the art regarding the specific parameters required to obtain the desired effect using gene therapy (obtaining adequate level of expression and/or targeting desired tissue to obtain desired effect) or regarding the specific combination of "immunostimulatory molecule" and antigen required to treat a specific type of cancer. It would require one of skill undue experimentation to determine the combination of "immunostimulatory molecule" and antigen using the claimed invention to treat a specific type of cancer.

3. Claims 1-20 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

The rejection of claim 1 regarding the metes and bounds of an "enhanced immunological response" is withdrawn because the phrase has been deleted.

Claims 1 and 9 remain indefinite because the phrase "heterologous boosting immunization" is unclear. It is unclear if the term "heterologous" indicates the vectors are foreign to the mammal, if the vectors are different than each other or if the vectors have different effects on the immune system. It is unclear if "boosting" occurs when either vector is administered or only after administration of the second vector.

Applicants argue pg 6-8, pg 18, lines 26-33 and Example 1, show the phrase specifically refers to administering a first vector followed by a second, different, boosting vector. Applicants argument is not persuasive. Page 6-8, pg 18, lines 26-33 and Example 1 discuss boosting with a second different vector encoding the same antigen. Injecting both vectors is not boosting as argued. The specification does not limit the second vector being administered as the "booster." In fact, since the mammal may have already been exposed to the virus in which case, the first vector may be a "booster." As written, it is not clear that "heterologous boosting immunization" as taught in the specification does not necessarily refer to administering two different vectors encoding the same antigen. Nor does the specification clearly limit "heterologous" booster immunization to the two vectors being different.

Claims 1 and 9 as newly amended are indefinite because it is unclear if "DNA [or viral] vector and a nucleic acid encoding said antigen" means the nucleic acid is part of the vector or if it is administered in addition to the vector.

Claim 1 as newly amended is indefinite because the metes and bounds of "antigen-associated disease" is unclear. It cannot be determined how a disease is associated with an antigen. Is a tumor expressing β-gal (Wang of record) an "antigen-associated disease?" Is any tumor an "antigen-associated disease" or only those in which an antigen that is specific to the tumor has been identified?

Claim 1 as newly amended is indefinite because treating "an antigen-associated disease" and obtaining an immune response against "at least one antigen" are not commensurate in scope.

Nor is obtaining an immune response against "at least one antigen" commensurate in scope with merely inducing an effective immune response.

Claims 1 and 8 are indefinite because it is not clear that the immune response induced is directed toward the antigen encoded by the vectors.

Claims 5 and 14 remain indefinite because it is unclear how the phrase "immunostimulatory molecule" further limit the claims. The vector in parent claims 1 and 9 encode an antigen and may encode viral proteins, both of which are immunostimulatory. Applicants argue the phrase encompasses antigens, tumor antigens, viral proteins, cytokines, restriction elements, co-stimulatory and accessory molecules (pg 8, line 6). Applicants argument is not persuasive because when the "immunostimulatory molecule" in claims 5 and 14 is an antigen, tumor antigen, viral protein, it is unclear if the antigen, tumor antigen, or viral protein is the antigen in claims 1 and 9 or if it is a second antigen in addition to the one in claims 1 and 9.

Claims 5 and 14 remain indefinite because nucleic acids do not encode any "immunostimulatory molecule" as claimed. The phrase encompasses "restriction elements, co-stimulatory and accessory molecules" (pg 8, line 24-26). However, the "restriction elements, co-stimulatory and accessory molecules" are not limited to proteins. Since nucleic acids do not encode restriction elements, co-stimulatory and accessory molecules that are not proteins, "molecule" should be changed to "protein".

Claim 9 as newly amended is unclear. It is unclear if the claim is limited to administering vectors to a patient having a tumor (treatment) or whether the claim encompasses administering

vectors to any patient. The phrase "the cancer in the patient" lacks antecedent basis in the claim because the patient does not have to have cancer.

Claim Rejections - 35 USC § 102

The rejection of claims 1-3, 5-7, 9, 14-16, 18 and 19 under 35 U.S.C. 102(a) as being anticipated by Chamberlain (April 20-24, 1996, Proc. Ann. Meeting American Assoc. Cancer Res, Vol. 37, abstract 3263) is withdrawn because Chamberlain is not "by others" as required under 35 U.S.C. 102(a).

Claim Rejections - 35 USC § 103

4. Claims 1-3, 5-7, 9, 14-16, 18 and 19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (J. Immunol., (1995 May 1) 154 (9) 4685-92) for reasons of record.

Wang taught administering a wild-type vaccinia virus to mice followed by administering a fowlpox virus encoding β-gal which caused an increase in CTL response in splenocytes as compared to administering wild-type vaccinia followed by vaccinia encoding β-gal (page 4689, col. 2, Fig. 6, 1st full para.). Wang did not teach administering vaccinia virus encoding β-gal followed by administering fowlpox virus encoding β-gal. However, Wang taught a vaccinia virus encoding β-gal. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to pre-immunize with vaccinia encoding β-gal followed by fowlpox encoding β-gal as taught by Wang. One of ordinary skill in the art at the time the invention was

made would have been motivated to replace wild-type vaccinia with vaccinia encoding β-gal to introduce the DNA encoding the antigen sooner while pre-immunizing.

Similarly, Wang taught administering a wild-type fowlpox followed by vaccinia encoding β-gal which also caused an immune response (page 4689, col. 2, 1st para.). Wang did not teach pre-immunizing with fowlpox encoding β-gal followed by vaccinia encoding β-gal. However, Wang taught administering fowlpox virus encoding β-gal caused an immune response. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to pre-immunize with fowlpox encoding β-gal followed by vaccinia encoding β-gal. One of ordinary skill in the art at the time the invention was made to replace wild-type fowlpox with fowlpox encoding β-gal to introduce the DNA encoding the antigen sooner while pre-immunizing.

Claim 5 is included because vaccinia virus encodes proteins that are immunostimulatory and because β-gal is an immunostimulatory molecule. Claims 9, 15 and 19 are included because the mere administration of two vectors is "treatment" as claimed; claim 9, 15 and 19 do not require any therapeutic effect.

Claims 9 is included because the limitation of producing an effective immune response against the cancer in the patient is equivalent to obtaining a CTL response in mice against CT26.CL26 (tumor cells expressing β-gal) as taught by Wang.

Applicants argue Wang did not teach administering wild-type vaccinia followed by fowlpox virus expressing β-gal did not diminish a response; therefore, applicants argue one

skilled in the art would have no motivation to modify the experiment in Fig. 6 of Wang. Applicants argue the skilled artisan reading Wang would not be motivated to inject a first vector encoding an antigen followed by a second, different vector encoding the same antigen. Applicants arguments are not persuasive. Applicants argument is not persuasive. Fig. 6, "VV/rFPV" clearly shows an increase in CTL response against β-gal expressing cells (CT26.CL25) when wild-type vaccinia is followed by FPV encoding β-gal. One of ordinary skill in the art at the time the invention was made would have been motivated to replace wild-type vaccinia (administered before FPV encoding β-gal) with vaccinia encoding β-gal to introduce the DNA encoding the antigen sooner in a pre-immunization. One of ordinary skill in the art at the time the invention was made to replace wild-type fowlpox (administered before VV encoding β-gal) with fowlpox encoding β-gal to introduce the DNA encoding the antigen sooner during pre-immunization.

Applicants argue Wang did not teach using a vector in the claimed method which enhances an immunological response by inoculating with different vectors each containing DNA encoding the same antigen. Applicants argument is not persuasive for reasons cited above, particularly because Fig. 6 shows 50% lysis of β-gal expressing cells, and because the claims do not require "enhancing" an immunological response.

5. Claims 1-3, 5-7, 9-11, 14-16, 18 and 19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (J. Immunol., (1995 May 1) 154 (9) 4685-92) for reasons of record.

Wang taught administering vaccinia encoding β-gal to mice followed by administering fowlpox encoding β-gal or vice versa which caused an immune response (see 103 rejection above). Wang did not expressly teach performing the method wherein β-gal is replaced with MART-1 or gp100. However, Wang suggested replacing β-gal with MART-1 and gp100 and taught making fowlpox virus encoding MART-1 and gp100 (page 4690, col. 2, last 2 para.). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the method of Wang wherein the β-gal gene is replaced with MART-1 or gp100 as suggested by Wang. One of ordinary skill in the art at the time the invention was made would have been motivated to replace β-gal with MART-1 or gp100 to determine if self proteins such as MART-1 or gp100 induced the same immune response as a foreign protein (β-gal) and to determine if MART-1 or gp100 enhanced the precursor frequency of T-cells that recognize MART-1 or gp100 prior to *ex vivo* expansion (page 4690, col. 2, para. 2, line 4).

Wang did not expressly teach performing the method wherein the vectors encode an immunostimulatory molecule. However, Wang taught adding a nucleic acid sequence encoding IL-2, IL-12, GM-CSF, et al. to the vectors encoding tumor antigens (page 4690, col. 2, 8 lines from the bottom). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the method of Wang wherein a nucleic acid sequence encoding an immunostimulatory molecule is added to the vectors encoding antigen. One of ordinary skill in the art at the time the invention was made would have been motivated to add a cytokine to the vectors at the suggestion of Wang.

Applicants do not provide any specific arguments why Wang does not teach the limitations of the claims or why motivation is lacking. The rejection has clearly set forth how Wang taught all the specific limitations of the claim and why one of ordinary skill in the art at the time the invention was made would have been motivated to replace β-gal with other antigens. As such, applicants arguments are moot.

6. Claims 1-3, 5-7, 9, 12-16, 18 and 19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (J. Immunol., (1995 May 1) 154 (9) 4685-92) in view of Orlow (1995, PNAS, Vol. 92, pages 10152-10156) for reasons of record.

Wang taught administering a vaccinia encoding β-gal, MART-1 or gp100 to mice followed by administering a fowlpox encoding β-gal, MART-1 or gp100 which caused an immune response against the antigen. Wang did not teach the method wherein the antigen is TRP-1 or TRP-2. However, Orlow taught the nucleic acid sequence of TRP-1 and TRP-2.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the method of Wang wherein the antigen was TRP-1 or 2 as taught by Orlow. One of ordinary skill in the art at the time the invention was made would have been motivated to replace MART-1 or gp100 with TRP-1 or 2 because MART-1, gp100, TRP-1 and 2 are all melanoma antigens. One of ordinary skill in the art at the time the invention was made would have been motivated to replace β-gal with TRP-1 or 2 to determine if self proteins such as TRP-1 or 2 induced the same immune response as a foreign protein (β-gal). One of ordinary skill in the

art at the time the invention was made would have been motivated to replace β-gal with TRP-1 or 2 to determine the precursor frequency of T-cells that recognize TRP-1 or 2 *in vivo*.

Applicants do not provide any specific arguments regarding why the combined teachings of Wang and Orlow do not teach the limitations of the claims or why motivation is lacking. As such, applicants arguments are moot. The rejection has clearly set forth how Wang and Orlow teach all the limitations of the claim and why one of ordinary skill in the art at the time the invention was made would have been motivated to combine the reference.

7. Claim 1-9 and 14-20 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (J. Immunol., (1995 May 1) 154 (9) 4685-92) in view of Zhai (Jan. 15, 1996, J. Immunol., Vol. 156, No. 2, pages 700-710) for reasons of record.

Wang taught administering a vaccinia virus encoding β-gal to a mice followed by administering a fowlpox virus encoding β-gal which caused an increase in CTL response in splenocytes as compared to administering two doses of vaccinia virus encoding β-gal. Wang did not teach replacing the vaccinia virus or fowlpox virus with an adenovirus. However, Zhai taught administering an adenoviral vector encoding β-gal to mice and obtaining an immune response.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the method of Wang wherein the vaccinia virus or fowlpox virus was replaced with the adenoviral vector taught by Zhai. One of ordinary skill in the art at the time the invention was made would have been motivated to replace the vaccinia virus (the first vector)

with the adenoviral vector to increase the CTL response against antigen as compared to administering adenoviral vector followed by readministration of adenoviral vector. One of ordinary skill in the art at the time the invention was made would have been motivated to replace the fowlpox virus (the second vector) with the adenoviral vector to determine if fowlpox was the only virus that could be used to obtain a CTL response against antigen after administering vaccinia virus.

Applicants do not provide any specific arguments regarding why the combined teachings of Wang and Zhai do not teach the limitations of the claims or why motivation is lacking. The rejection has clearly set forth how Wang and Zhai teach all the limitations of the claim and why one of ordinary skill in the art at the time the invention was made would have been motivated to combine the reference. As such, applicants arguments are moot.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of formal matters can be directed to the patent analyst, Dianiece Jacobs, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-3388.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael C. Wilson

MICHAEL C. WILSON
PATENT EXAMINER